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| 09/718,102 | 11-20-2000 | Maria-Grazia Roncarolo | DX0261K1B | 9698 |

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[REDACTED] EXAMINER

HAMUD, FOZIA M

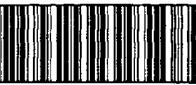
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1647

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Please find below and/or attached an Office communication concerning this application or proceeding.

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|---|---|--|--|--|--|---|---|--|
| Office Action Summary | Application No. 09/718,102 | Applicant(s) Roncarolo et al | | | | | | |
| | Examiner Fozia Hamud | Art Unit 1647 | | | | | | |
| |  | | | | | | | |
| <i>-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --</i> | | | | | | | | |
| Period for Reply A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE <u>3</u> MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION. <ul style="list-style-type: none"> - Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication. - If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely. - If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication. - Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). - Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b). | | | | | | | | |
| Status <p>1) <input checked="" type="checkbox"/> Responsive to communication(s) filed on <u>Sep 17, 2002</u>.</p> <p>2a) <input type="checkbox"/> This action is FINAL. 2b) <input checked="" type="checkbox"/> This action is non-final.</p> <p>3) <input type="checkbox"/> Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under <i>Ex parte Quayle</i>, 1935 C.D. 11; 453 O.G. 213.</p> | | | | | | | | |
| Disposition of Claims <p>4) <input checked="" type="checkbox"/> Claim(s) <u>2-5 and 15-27</u> is/are pending in the application.</p> <p>4a) Of the above, claim(s) _____ is/are withdrawn from consideration.</p> <p>5) <input type="checkbox"/> Claim(s) _____ is/are allowed.</p> <p>6) <input checked="" type="checkbox"/> Claim(s) <u>2-5 and 15-27</u> is/are rejected.</p> <p>7) <input type="checkbox"/> Claim(s) _____ is/are objected to.</p> <p>8) <input type="checkbox"/> Claims _____ are subject to restriction and/or election requirement.</p> | | | | | | | | |
| Application Papers <p>9) <input type="checkbox"/> The specification is objected to by the Examiner.</p> <p>10) <input type="checkbox"/> The drawing(s) filed on _____ is/are a) <input type="checkbox"/> accepted or b) <input type="checkbox"/> objected to by the Examiner. Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).</p> <p>11) <input type="checkbox"/> The proposed drawing correction filed on _____ is: a) <input type="checkbox"/> approved b) <input type="checkbox"/> disapproved by the Examiner. If approved, corrected drawings are required in reply to this Office action.</p> <p>12) <input type="checkbox"/> The oath or declaration is objected to by the Examiner.</p> | | | | | | | | |
| Priority under 35 U.S.C. §§ 119 and 120 <p>13) <input type="checkbox"/> Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).</p> <p>a) <input type="checkbox"/> All b) <input type="checkbox"/> Some* c) <input type="checkbox"/> None of:</p> <ol style="list-style-type: none"> 1. <input type="checkbox"/> Certified copies of the priority documents have been received. 2. <input type="checkbox"/> Certified copies of the priority documents have been received in Application No. _____. 3. <input type="checkbox"/> Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)). <p>*See the attached detailed Office action for a list of the certified copies not received.</p> | | | | | | | | |
| <p>14) <input type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).</p> <p>a) <input type="checkbox"/> The translation of the foreign language provisional application has been received.</p> <p>15) <input checked="" type="checkbox"/> Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.</p> | | | | | | | | |
| Attachment(s) <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 33%;">1) <input type="checkbox"/> Notice of References Cited (PTO-892)</td> <td style="width: 33%;">4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____</td> </tr> <tr> <td>2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)</td> <td>5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)</td> </tr> <tr> <td>3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s).</td> <td>6) <input type="checkbox"/> Other: _____</td> </tr> </table> | | | 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s). _____ | 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) | 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). | 6) <input type="checkbox"/> Other: _____ |
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| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449) Paper No(s). | 6) <input type="checkbox"/> Other: _____ | | | | | | | |

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DETAILED ACTION

1a. Receipt of Applicant's arguments and amendments filed in Paper No.11, 17 September 2002 is acknowledged. Claims 2, 15, 19 and 20 have been amended. Claims 2-5 and 15-27 are pending and under consideration by the Examiner.

2. The following previous objections and rejections are withdrawn in light of Applicants amendments filed in Paper No.11, 09/17/02:

(I) The objection to the title.

(II) The rejection of claims 2-5, 15-19, made under 35 U.S.C. §102(b), as being anticipated by Rott et al, because Applicants provide support for the claimed invention in their prior Application filed on 03/04/1992.

(III) The rejection of claims 20-22, made under 35 U.S.C. §112, first paragraph. (Examiner stands corrected that claims 24-27 were inadvertently included in the rejection made under 35 U.S.C. §112, first paragraph).

(IV) The rejection of claims 3, 4, 19 and 20, made under 35 U.S.C. §112, second paragraph.

1b. Applicant is thanked for providing the 1449 form listing all of the references. Applicant is also thanked for correcting the priority data.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Applicant's arguments filed in Paper No.11, 09/17/02, have been fully considered but were deemed persuasive in part. The issues remaining as well as new issues are restated below.

Claim Rejections-35 USC § 112

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5. Claim 23 stands rejected under 35 U.S.C. 112, second paragraph for reasons of record set forth in Paper No:10 (7/30/02), section 4a on pages 3-5.

Applicants argue that claims 20-23 merely specify that the immune response recited in claim 15 accompanies tissue transplantation, and is therefore, distinguished from a claim that recites "inhibiting tissue rejection". The rejection against claims 20-22 made under 35 U.S.C. §112, first paragraph is withdrawn. However, the rejection of claim 23 made under 35 U.S.C. §112, first paragraph, is maintained, because instant specification does not provide enablement for introducing T cells to the recipient or administering IL-10 to the tissue to be transplanted before transplantation, as recited in claim 23 (b) and (c). Instant specification asserts that often, when a response accompanies tissue transplantation, the T cell is introduced to the recipient, or IL-10 is administered to the tissue to be transplanted, before transplantation, (see page 5, lines 1-10). However, the specification does not disclose the introduction of T cells to a recipient or administering IL-10 to a tissue to be transplanted. While, expanding T cells ex-vivo and introducing them to a recipient might one day be a feasible therapy for tissue transplant patients, this type of therapy is still in early stages of research, and Applicants have not shown that it is effective. Also researchers continue to study various ways to fool the immune system into accepting foreign tissues or to take advantage of the immune response, and while administering IL-10 into the tissue to be transplanted might one day be a feasible therapy, however, this specification have not shown that the this an effective and save way of suppressing said immune response. Instant specification speculates that the administration of IL-10 to a tissue to be transplanted might be an option for suppressing immune response which accompany tissue

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transplantation, however, it provides no evidence that this is safe and effective way of suppressing said immune response. Therefore, Applicants have not provided enablement for introducing T cells to the recipient or administering IL-10 to the tissue to be transplanted before transplantation, as recited in claim 23 (b) and(c).

6. The rejection of claims 2, 5 and 15 under 35 U.S.C. 112, second paragraph is maintained for reasons of record set forth in Paper No:10 (7/30/02), section 4a on pages 5-7.

6a. Applicants argue that amended claim 2 is clear and is directed to inhibiting an antigen-specific response of an immune system by administration of IL-10 and an antigen, (i.e, in vivo activity). This argument is not found persuasive, because it is unclear who or what is the IL-10 being administered to. Claim 2 recites “..... comprising administering to said immune system an effective amount of”, however, it is unclear how to administer IL-10 to an immune system. It is unclear whether the immune system is in a subject, and if so, what subject, an animal or a human. Thus, if the claim is drawn to a method of inhibiting an antigen-specific response by administering IL-10, it should recite what subject is the IL-10 being administered to.

6b. With respect to claim 5, Applicants argue that it is clear that administration of IL-10 also leads to reduced stimulatory activity of the recited cells on T cell activation. Although, instant specification does disclose that IL-10 leads to reduced capacity of PBMC, monocytes and normal B cells in stimulating T cells, however, the way claim 5 is written, it is unclear that stimulatory capacity of the recited cells is on T cells.

6c. With respect to claim 15, Applicants assert that the claim is directed to suppressing an immune response of a T cell to an antigen by administration of IL-10 and the antigen or an anti-

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CD3 antibody. However, it is unclear, how are the combination of IL-10 and either the antigen or anti-CD3 be administered into a cell. Again it's unclear, whether the cell is in a subject or in a petri dish.

Claims 16-24 are rejected as being vague and indefinite, so far as they depends on claim 15, for the limitation set forth directly above.

New Rejections:

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7a. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of inhibiting stimulation of T cells by specific antigen, said method comprising administering to a subject IL-10 and an antigen, does not reasonably provide enablement for a method of inhibiting "all" possible antigen-specific responses of an immune system by administering IL-10 and an antigen. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

Instant claim 2 is directed to a method of inhibiting "all" possible immune responses due to an antigen by administering IL-10 and an antigen, however, instant specification teaches that IL-10 induces T cell anergy in alloantigen-specific and anti-CD3 stimulated CD4+ T cells , and inhibits the production of IL-2, IFN- γ , IL-5, TNF- α , GM-CSF by these cells, (see page 53, line

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27 through page 54 line 19, 59, lines 5-30). The specification discloses that IL-10 renders T cells anergic and this is not reversed by addition of IL-2, and that the signaling through the TCR/CD3 complex is selectively impaired in IL-10 anergized T cells, (page 59, lines 31-36). Instant claim 2 encompasses the inhibition of an immune response induced by an antigen, by administering IL-10 and said antigen, however, the claim does not differentiate whether this immune response is humoral or cell mediated. Instant specification only teaches that the immune response inhibited by the administration of IL-10 an antigen, is an immune response that is mediated by T cells.

The criteria set forth in *Ex parte Forman* (230 USPQ 546 (Bd. Pat. App. & Int. 1986), and reiterated in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)), which include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art and (8) the breadth of the claims, is the basis for determining undue extirmination. In the instant application, it would be unpredictable whether the administration to a subject of a combination of IL-10 and an antigen, would lead to inhibition of "all" possible antigen induced immune responses, (i.e., both humoral and cell mediated), because immune responses induced by particular antigens invoke different effector mechanisms, and there are severe consequences if an incorrect immune response is induced or suppressed. Thus, while the administration of IL-10 and an antigen might lead to the inhibition of T cell mediated immune response, it may have no effect at all, or even be harmful to a subject suffering from an antigen that induces an immune response mediated by a different mechanism. Therefore, one of ordinary

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skill in the art would not be able to predict whether the administration of IL-10 with or an antigen would inhibit an immune response the is not mediated by T cell, given the lack of guidance by instant specification. Therefore, instant specification is enabling for a method of inhibiting stimulation of T cells by specific antigen, said method comprising administering to a subject IL-10 and an antigen.

Claims 2-5 are rejected under 35 U.S.C. 112, first paragraph, so far as they depends on claim 2, for the limitation set forth directly above.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7a. Claims 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

7b. Claim 25 recites “a method of suppressing a subsequent response in a T cell to an antigen, comprising administering to an immune system comprising said cell.....”, however , it is unclear, how are the combination of IL-10 and either the antigen or anti-CD3, be administered into an immune system, does this mean that said combination is administered into a subject?. Appropriate correction is required.

7c. Claim 27 recites “a method of inducing in a T cell anergy to an MHC antigen comprising administering to a precursor to said T cell.....”, which renders the claim vague, because, the meaning of “precursor to said T cell” is unclear. Appropriate correction is required.

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Claim 26 is rejected as being vague and indefinite, so long as it depends on claim 25, for the limitation set forth above.

Conclusion

8. No claim is allowable. The invention is free of the prior art of record.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fozia Hamud whose telephone number is (703) 308-8891. The examiner can normally be reached on Mondays-Thursdays from 8:00AM to 4:30PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary kunz can be reached at (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4227. Faxed draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Fozia Hamud
Patent Examiner
Art Unit 1647
27 November 2002

Gary L. Kunz
GARY KUNZ
SUPERVISORY PATENT EXAMINER
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